HYBRID-IMAGING SPECTROMETER

Cross-Reference to Related Application

~~This application is a continuation-in-part of a United States patent application~~ entitled "Hybrid-Scanning Spectrometer" ~~filed~~ March 26, 2001, serial no. _________, ~~which is herein incorporated by reference.~~

Field of the Invention

This invention pertains to spectrometers, and more particularly to imaging spectrometers that operate according to hybrid scanning methods.

Background of the Invention

Imaging spectrometers have been applied to a variety of disciplines, such as the detection of defects in industrial processes, satellite imaging, and laboratory research. These instruments detect radiation from a sample and process the resulting signal to obtain and present an image of the sample that includes spectral and chemical information about the sample. A few imaging spectrometers have been proposed that employ a variable-bandwidth filter. Such spectrometers generally include dispersive elements to limit the spectral information received by the array, or slits, apertures, or shutters to limit the spatial information received by the array.

Summary of the Invention

Several aspects of the invention are presented in this application. These are applicable to a number of different endeavors, such as laboratory investigations, microscopic imaging, infrared, near-infrared, visible absorption, Raman and fluorescence spectroscopy and imaging, satellite imaging, quality control, industrial process monitoring, combinatorial chemistry, genomics, biological imaging, pathology, drug discovery, and pharmaceutical formulation and testing.

Systems according to the invention are advantageous in that they can perform precise spectral imaging and computation with a robust and simple instrument. By acquiring a scanned series of mixed spectral images and then deriving pure spectral

images from them, systems according to the invention can be made with few moving parts or more robust mechanisms than prior art systems. This is because they can be made using a simple variable optical filter in place of more costly interferometers, or active variable filters such as liquid crystal tunable filters (LCTF). The resulting systems can therefore be less expensive and more reliable.

Systems according to the invention can also acquire images with more efficiency because their detector arrays have a field of view that is not obstructed by slits or shutters and the average optical throughput of the filter is greater than other active tunable filter approaches. As a result, systems according to the invention need not suffer from the problems that tend to result from high levels of illumination, such as excessive heating of the sample, and the cost and fragility of high intensity illumination sources.

<u>Brief Description of the Drawings</u>

Fig. 1 is a diagram of an illustrative embodiment of an imaging spectrometer according to the invention, including a perspective portion illustrating the relationship between its image sensor, its variable filter, its actuator, and its sample area;

Fig. 2 is a plan view diagram of an image sensor for use with the process control system of Fig. 1;

Fig. 3 is a plan view diagram illustrating output of the system of Fig. 1;

Fig. 4 is a flowchart illustrating the operation of the embodiment of Fig. 1;

Fig. 5 is sectional diagram illustrating the sequential acquisition of a series of mixed spectral images of a sample with an embodiment of the invention in which the variable filter moves;

Fig. 6 is sectional diagram illustrating the sequential acquisition of a series of mixed spectral images of a sample with an embodiment of the invention in which the sample moves; and

Fig. 7 is a block diagram of another embodiment according to the invention, which is an example of a fluorescence measurement instrument that uses two variable filters.

In the figures, like reference numbers represent like elements.

Description of an Illustrative Embodiment

Referring to Fig. 1, an optical instrument according to the invention, features a two-dimensional array sensor 10 and a spatially-variable filter 12, such as a variable-bandpass filter, facing a sample area 16. The sample area can be a continuous area to be imaged, such as a tissue sample, or it can include a number of discrete sub-areas 18. These sub-areas can take on a variety of forms, depending on the type of instrument. In a macroscopic diagnostic instrument, for example, the sample areas can each be defined by one of a number of sample vessels. And in a microscopic instrument, the areas might be a number of reaction areas on a test chip. The instrument can also be used to examine a series of pharmaceutical dosage units, such as capsules, tablets, pellets, ampoules, or vials, or otherwise combined with the teachings described in applications entitled "High-Volume On-Line Spectroscopic Composition Testing of Manufactured Pharmaceutical Dosage Units," including application no. 09/507,293, filed on February 18, 2000, application no. 60/120,859, filed on February 19, 1999, and application no. 60/143,801, filed on July 14, 1999, which are all herein incorporated by reference. The concepts presented in this application can also be combined with subject matter described in applications entitled "High-Throughput Infrared Spectrometry," including application no. 09/353,325, filed July 14, 1999, application no. 60/092,769 filed on July 14, 1998, and application no. 60/095,800 filed on August 7, 1998, all of which are herein incorporated by reference, as well as applications entitled "Multi-Source Array," including application no. 60/183,663, filed on February 18, 2000, and application no. 09/788,316, filed on February 16, 2001, which are both herein incorporated by reference.

Where multiple sub-areas are used, the image sensor is preferably oriented with one or both of its dimensions generally along an axis that is parallel to the spatial distribution of sample elements. Note that the instrument need not rely on a predetermined shape for the elements, but instead relies on the fact that the actuator motion and acquisition are synchronized by the instrument.

The filter 12 has a narrow pass-band with a center wavelength that varies along one direction. The leading edge A of the filter passes shorter wavelengths, and as the distance from the leading edge along the process flow direction increases, the filter passes successively longer wavelengths. At the trailing edge N of the filter, the filter passes a

narrow range of the longest wavelengths. The orientation of the filter can also be reversed, so that the pass-band center wavelength decreases along the process flow direction. Although the filter has been illustrated as a series of strips located perpendicular to the process flow direction, it can be manufactured in practice by continuously varying the dielectric thickness in an interference filter. Preferably, the filter should have a range of pass-bands that matches the range of the camera. Suitable filters are available, for example, from Optical Coatings Laboratory, Inc. of Santa Rosa, California. The variable filter can be located between the sample and the detector or between the source and sample. In a microscopic application, for example, the actuator can move the variable filter between the source and the sample, before light interacts with the sample. Alternatively, with the same optical configuration, the sample could be moved to achieve the same effect.

Referring to Fig. 2, the image sensor 10 is preferably a two-dimensional array sensor that includes a two-dimensional array of detector elements made up of a series of lines of elements (A1 - An, B1 - Bn, ... N1 – Nn) that are each located generally along an axis that is perpendicular to the spatial distribution of sample elements. The image sensor can include an array of integrated semiconductor elements, and can be sensitive to infrared radiation. Other types of detectors can also be used, however, such as CCD detectors that are sensitive to ultraviolet light, or visible light. For near infrared applications, uncooled two-dimensionsal Indium-Gallium-Arsenide (InGaAs) arrays, which are sensitive to near-infrared wavelengths, are suitable image sensors, although sensitivity to longer wavelengths, such as Mercury-Cadmium-Telluride (MCT) would also be desirable. It is contemplated that the sensors should preferably have dimensions of at least 64 x 64 or even 256 x 256.

The system also includes an image acquisition interface 22 having an input port responsive to an output port of the image sensor 10. The image acquisition interface receives and/or formats image signals from the image sensor. It can include an off-the shelf frame grabber/buffer card with a 12-16 bit dynamic range, such as are available from Matrox Electronic Systems Ltd. of Montreal, Canada, and Dipix Technologies, of Ottawa, Canada.

A spectral processor 26 has an input responsive to the image acquisition interface 22. This spectral processor has a control output provided to a source control interface 20, which can power and control an illumination source 14, which can be placed to reflect light off the sample or transmit light through the sample. The illumination source for near-infrared measurements is preferably a Quartz-Tungsten-Halogen lamp. For Raman measurements, the source may be a coherent narrow band excitation source such as a laser. Other sources can of course also be used for measurements made in other wavelength ranges.

The spectral processor 26 is also operatively connected to a standard input/output (IO) interface 30 and may also be connected to a local spectral library 24. The local spectral library includes locally-stored spectral signatures for substances, such as known process components. These components can include commonly detected substances or substances expected to be detected, such as ingredients, process products, or results of process defects or contamination. The IO interface can also operatively connect the spectral processor to a remote spectral library 28.

The spectral processor 26 is operatively connected to an image processor 32 as well. The image processor can be an off-the-shelf programmable industrial image processor, that includes special-purpose image processing hardware and image evaluation routines that are operative to evaluate shapes and colors of manufactured objects in industrial environments. Such systems are available from, for example, Cognex, Inc.

An actuator 15 can be provided to move the filter 12 using a motive element, such as a motor, and a mechanism, such as a linkage, a lead screw, or a belt. The actuator is preferably positioned to move the filter linearly in the same direction along which its characteristics vary, or at least in such a way as to provide for at least a component of motion in this direction. In a related embodiment, the actuator moves the sample, such as by moving a sample platform. It may even be possible in some embodiments to move the camera or another element of the instrument, such as an intermediate mirror, if the arrangement allows for radiation from one sample point to pass through parts of the filter that have different characteristics before reaching the detector. In the present embodiment, the actuator includes a computer controlled motorized translation stage such as is available from National Aperture, of Salem, NH.

The actuator can be a precise open-loop actuator, or can provide for feedback. Open loop actuators, such as precise stepper motors, allow the system to precisely advance the filter during acquisition. Feedback-based systems provide for a position or velocity sensor that indicates to the system the position of the filter. This signal can be used by the system to determine the position or velocity of the filter, and may allow the system to correct the filter scanning by providing additional signals to the actuator. The actuator can be designed to move the filter in a stepped or continuous manner.

In one embodiment, the system is based on the so-called IBM-PC architecture. The image acquisition interface 22, IO interface 30, and image processor 32 each occupy expansion slots on the system bus. The spectral processor is implemented using special-purpose spectral processing routines loaded on the host processor, and the local spectral library is stored in local mass storage, such as disk storage. Of course, other structures can be used to implement systems according to the invention, including various combinations of dedicated hardware and special-purpose software running on general-purpose hardware. In addition, the various elements and steps described can be reorganized, divided, and combined in different ways without departing from the scope and spirit of the invention. For example, many of the separate operations described above can be performed simultaneously according to well-known pipelining and parallel processing principles.

In operation, referring to Figs. 1-4, the array sensor 10 is sensitive to the radiation that has interacted with the whole surface of the sample area 16, and focused or otherwise imaged by a first-stage optic, such as a lens (not shown). In operation of this embodiment, the acquisition interface 22 acquires data representing a series of variably-filtered, two-dimensional images. These two-dimensional images each include image values for the pixels in a series of adjacent lines in the sample area. Because of the action of the variable-bandpass filter, the detected line images that make up each two-dimensional image will have a spectral content that varies along one of the image axes.

One or more of the sample areas can include a reference sample. These sample areas can be located at fixed positions with respect to the other sample areas, or they can be located in such a way that they move with the scanning element of the instrument. This implementation can allow for the removal of transfer of calibration requirements

between systems by simultaneously collecting reference spectra for spectral comparison. Referring to Fig. 4, spectral images can be assembled in a two-stage process. The first stage of the process is an acquisition stage, which begins with the acquisition of a first hybrid image of the sample S (step 40). The actuator is then energized to move the filter relative to the sample by a one pixel wide increment, and another mixed image is acquired. This part of the process can be repeated until the filter has been scanned across the whole image (step 42). At the end of this process stage, the system will have acquired a three-dimensional mixed spectral data set.

In the second stage image data are extracted from the mixed spectral data set and processed. In the embodiment described, pure spectral images are extracted in the form of a series of line images acquired at different relative positions (steps 46 and 48). Part or all of the data from the extracted line image data sets can then be assembled to obtain two-dimensional spectral images for all or part of the sample area and pure spectra for each pixel in the image

The conversion can take place in a variety of different ways. In one approach, a whole data set can be acquired before processing begins. This set can then be processed to obtain spectral images at selected wavelengths. The instrument may also allow a user to interact with an exploratory mode, in which he or she can look at representations of any subset of the data. This can allow the user to zoom in to specific parts of the sample and look at wavelengths or wavelength combinations that may not have been contemplated before the scan.

Data can also be processed as scanning of the filter occurs. In this approach, data may be processed or discarded as it is acquired, or simply not retrieved from the detector to create an abbreviated data set. For example, the instrument may only acquire data for a certain subset of wavelengths or areas, it may begin spectral manipulations for data as they are acquired, or it may perform image processing functions, such as spatial low-pass filtering, on data as they are acquired. Adaptive scanning modes may also be possible in which the instrument changes its behavior based on detected signals. For example, the instrument can abort its scan and alert an operator if certain wavelength characteristics are not detected in a reference sample.

In one example, the data can be accumulated into a series of single-wavelength bit planes for the whole image, with data from these bit planes being combined to derive spectral images. Data can also be acquired, processed, and displayed in one fully interleaved process, instead of in the two-stage approach discussed above. And data from the unprocessed data set can even be accessed directly on demand, such as in response to a user command to examine a particular part of the sample area, without reformatting the data as a whole.

Referring to Fig. 5, the data set 60 will be acquired differently depending on which part or parts of the instrument are designed to move. In an instrument where a filter 12 moves in front of a stationary sample area 16, for example, the same line of detector array elements will acquire line images within different acquired image planes (I1, I2, ... Iz) at different wavelengths (λ1, λ2, ... λn) for the each part of the sample area (x1, x2, ... xn) as the filter moves between the array and the sample area. The line images for a line on the sample will therefore be "stacked" in the data set. Substantially all of the data planes for the images will be only partially filed, however, and there will be twice as many images as needed. It may therefore be desirable to "square out" the data set into a right-angled array by shifting data, either as its is acquired and stored, or as a dedicated post-acquisition step.

Referring to Fig. 6, in instruments where a sample area 16 moves in front of a stationary filter 12, the different lines of detector array elements will always acquire line images at a same respective wavelength (λ1, λ2, ... λn). These acquisitions will be for different lines (x1, x2, ... xn) of the sample area, however, as the sample moves. In this case, therefore, the line images for a single line on the sample will be offset along a diagonal (e.g., xn-xn- ... –xn) through the data set 60. For this reason it may also be a good idea to "square out" the data set in these types of instruments.

The examples presented above assume that the filter is advanced by increments that each correspond to one row of pixels in the array. Other progressions are also possible, such as systems that move in sub-row (or multi-row) increments. And continuous systems may deviate significantly from their ideal paths, especially at the end of a scan. The specific nature of a particular instrument must therefore be taken into consideration in the designing of an acquisition protocol for a particular system.

Once the spectral images are assembled, the spectral processor 26 evaluates the acquired spectral image cube. This evaluation can include a variety of univariate and multivariate spectral manipulations. These can include comparing received spectral information with spectral signatures stored in the library, comparing received spectral information attributable to an unknown sample with information attributable to one or more reference samples, or evaluating simplified test functions, such as looking for the absence of a particular wavelength or combination of wavelengths. Multivariate spectral manipulations are discussed in more detail in "Multivariate Image Analysis," by Paul Geladi and Hans, Grahn, available from John Wiley, ISBN No. 0-471-93001-6, which is herein incorporated by reference.

As a result of its evaluation, the spectral processor 26 may detect known components and/or unknown components, or perform other spectral operations. If an unknown component is detected, the system can record a spectral signature entry for the new component type in the local spectral library 24. The system can also attempt to identify the newly detected component in an extended or remote library 28, such as by accessing it through a telephone line or computer network. The system then flags the detection of the new component to the system operator, and reports any retrieved candidate identities.

Once component identification is complete, the system can map the different detected components into a color (such as grayscale) line image. This image can then be transferred to the image processor, which can evaluate shape and color of the sample or sample areas, issue rejection signals for rejected sample areas, and compile operation logs.

As shown in Fig. 3, the color image will resemble the sample area, although it may be stretched or squeezed in the direction of the actuator movement, depending on the acquisition and movement rates. The image can include a color or grayscale value that represents a background composition. It can also include colors or grayscale values that represent known good components or component areas18A, colors that represent known defect components 18B, and colors or grayscale values that represent unknown components 18C. The mapping can also take the form of a spectral shift, in which some or all of the acquired spectral components are shifted in a similar manner, preserving the

relationship between wavelengths. Note that because the image maps components to colors or grayscale values, it provides information about spatial distribution within the sample areas in addition to identifying its components.

While the system can operate in real time to detect other spectral features, its results can also be analyzed further off-line. For example, some or all of the spectral data sets, or running averages derived from these data sets can be stored and periodically compared with extensive off-line databases of spectral signatures to detect possible new contaminants. Relative spectral intensities arising from relative amounts of reagents or ingredients can also be computed to determine if the process is optimally adjusted.

Referring to Fig. 7, spectrometers according to the invention can also use more than one variable filter oriented in the same or a different direction. For example, in the embodiment shown in Fig. 7, a first filter 72 can filter radiation from a source 70 before it interacts with a sample 74. A second, different, filter 76 is rotated by 90 degrees about the optical axis with respect to the first filter. In this embodiment, the second filter and a detector 78 are also positioned such that the second filter will filter light received at a right angle from the sample before it is detected by the detector 78. The two filters are therefore part of the same the optical path from the detector, where that optical path can be bent at various angles or straight. This embodiment can be used in fluorescence measurements, with the first filter filtering the excitation wavelengths and the second filter filtering the emitted wavelengths, although other types of multi-filter embodiments can also be constructed. Embodiments of type shown in Fig. 7 can be used for two-dimensional fluorescence measurements (i.e. to make an excitation v. emission map) of a single uniform sample without moving any elements, or images may be obtained by scanning one or more of the elements of the apparatus in one or more directions.

In one embodiment, the spectrometer can be equipped with an additional magnifying optic that can be used to focus further in to specific points of interest within the instrument's field of view. This lens can even be such that it causes light from a single point on the sample to be incident across the entire filter and array, resulting in a single point "point-and-shoot" spectrometer in which the filter or sample do not need to be moved.

The present invention has now been described in connection with a number of specific embodiments thereof. However, numerous modifications which are contemplated as falling within the scope of the present invention should now be apparent to those skilled in the art. Therefore, it is intended that the scope of the present invention be limited only by the scope of the claims appended hereto. In addition, the order of presentation of the claims should not be construed to limit the scope of any particular term in the claims.

What is claimed is: